IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

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|---|---|
| KIMBERLY C. CUTONE and, ANTHONY CUTONE<br><br>Plaintiffs,<br><br>v.<br><br>ELI LILLY AND COMPANY,<br><br>Defendant. | Civil Action No. 04-CV-12725 (JLT) |

**AFFIDAVIT OF AARON M. LEVINE, ESQ.**
**REGARDING AUTHENTICATION OF DOCUMENTS**

I, Aaron M. Levine, declare under penalty of perjury that the following is true and correct:

1. Attached as Exhibit 1 is a true copy of the Statement of Harold B. Sparr, R.Ph., dated May 16, 2006.

2. Attached as Exhibit 2 is a true copy of the Report of Hannelore Vanderschmidt, Ph.D., Ed.M., dated August 26, 2004, and a Letter from Hannelore Vanderschmidt, Ph.D. agreeing to write said Report, dated April 13, 2004.

3. Attached as Exhibit 3 is a true copy of the Affidavit of Aaron M. Levine Regarding Identification, dated July 5, 2006.

4. Attached as Exhibit 4 is a true copy of A Phase II Study of a Combination of Pemetrexed and Gemcitabine in Patients with Metastic Breast Cancer: An NCCTG Study by Eli Lilly & Company (approved Jan. 27, 2006).

5. Attached as Exhibit 5 is a true copy of the deposition of Mrs. Virginia Camporesi in Kimberly C. Cutone and Anthony Cutone v. Eli Lilly and Company, et al., No. 04-CV-1365 (D.D.C. 2004) at pp. 32, 36-37, 45, 47-48, 55, dated October 27, 2005.

6. Attached as Exhibit 6 is a true copy of pages 224, 819-20 of the Physicians Desk Reference to Pharmaceutical Specialties and Biologicals (Medical Economics, Inc., 23rd ed. 1969).

7. Attached as Exhibit 7 is a true copy of Eli Lilly and Company's Warehousing and Distribution Service Agreement for Wholesalers, dated July 1, 1970.

I declare under the penalty of perjury that the foregoing is true and correct.

/s/ Aaron M. Levine
Aaron M. Levine

Dated: July 6, 2006

**CERTIFICATE OF SERVICE**

I, Erica Tennyson, hereby certify that this Affidavit of Aaron M. Levine, Esq. Regarding Authentication of Documents, filed in support of Plaintiff's Opposition to Defendant Eli Lilly's Motion to Strike the Statement of Harold Sparr, R.Ph., filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non registered participants on July 11, 2006.

/s/ Erica Tennyson
Erica Tennyson

**STATEMENT OF HAROLD SPARR, R. PH.**

Harold B. Sparr declares under penalty of perjury that the following is true and correct:

1. I am a registered and licensed pharmacist in Massachusetts, New York, and California having graduated in 1951 from the Massachusetts College of Pharmacy. I have continuously and exclusively engaged in pharmacy from 1944 to the present.

2. I was the President of the Massachusetts Board of Registration in Pharmacy as well as the President of the Massachusetts College of Pharmacy Alumni Association, and as such am personally familiar with registered pharmacists in the Boston region, as well as the actual practice of pharmacy and retail pharmaceutical catalogues.

3. From the year 1944 to the present, I have worked at the following local Boston pharmacies:

A) Sparr's Drug Store, Inc. on 635 Huntington Ave., Boston, MA. (1944-1969);

B) Ivy Drug on Park Drive, Boston, MA (1955);

C) Jacobson's Pharmacy on Harvard Street, Boston (Dorchester),MA. (1955-1956);

D) Robert's Pharmacy on 360 Trapelo Road., Belmont, MA (1969-1976).

4. I was a member of Boston Association of Retail Pharmacists (now called Massachusetts Independent Pharmacists Association) from 1955 to the present. I have had the opportunity to meet with, work with, and discuss the practice of pharmacy with hundreds of pharmacists in Suffolk County, especially in Boston, over the last fifty years.

5. I am familiar with those pharmaceuticals commonly used for the care and treatment of pregnant women in the late 1960's and early 1970's in the Boston area, including Allston. I am also familiar with the pharmacy literature in the marketing of drugs in the 1960's and 1970's.

6. I am familiar with the Red and Blue Books and those publications' listings of many diethylstilbestrol (DES) manufacturers besides Eli Lilly in the 1960's and 1970's. However, while the Red and Blue Books may represent all the medications in the world, they have no relevance to the Boston areas as Lilly virtually owned that DES market in the 1960's and 1970's.

7. I am familiar with the practice of stocking and dispensing of DES in the 1960's and 1970's in Boston. In the 1960's and 1970's, generics were not popular and were disfavored in the trade since they did not have the quality control of the major brands. Because Lilly was top quality, the Lilly DES drug was inexpensive, and could be ordered from a Lilly wholesaler one bottle at a time, the drugstores in Boston stocked Lilly's DES exclusively.

8. Based upon my practice, experience, and observations of the practice of pharmacy in Allston in the 1960's and 1970's, if a woman was dispensed DES as a white, round, cross-scored tablet in 1969-1970, she would have received Lilly's Diethylstilbestrol, as that was the only popular brand at that time in pill form in that place.

9. The import and design of the Red and Blue Books as it pertains to DES reflects a picture of the myriad and numerous regional generic bottlers of this chemical in

the various cities and localities in America representing fifty different states and over a 100 different cities.

10. The Red and Blue Books do not represent nor were they designed to represent the availability of DES in the Boston market.

11. The great number or the great majority of the DES companies listed were not manufacturers of DES but only repackagers in local limited markets. That is, a pharmacist would repackage DES under his own label and sell it as a generic to pharmacists in this area. Of the brands listed, only a few were national pharmaceutical distributors. I.e. Lilly, Squibb, Merck, Upjohn, or Pfizer. The others were not national distributors and were not in Boston, Massachusetts. 90% of the names listed under Red and Blue Book are local generic repackagers of DES. Lilly was the Microsoft of those days.

I declare under the penalty of perjury that the foregoing is true and correct based on my personal knowledge.

Harold B. Sparr, R. PH.

Witness

210 Mahanton St #121
Newton, Mass. 02459
Address

Dated: May 16, 2006

Boston University

Center for Educational Development in Health
53 Bay State Road
Boston, Massachusetts 02215
617/353-4528
Fax: 617/353-7417
E-mail: asegall@bu.edu
hvanders@bu.edu

April 13, 2004

To whom it may concern

I agree to analyze, aggregate and summarize data from the pharmacist's survey regarding dispensing of Dyethylstilbestrol (DES) in the 1960's. Three hundred surveys are being sent out to Massachusetts' pharmacists who practiced in the 1960s. Remedy Pharmacy When surveys are returned, Management Services, Inc will send the completed surveys to me for analysis.

I will summarize each respondent's survey as follows:

- Name and address of pharmacist
- Pharmacy school attended
- When licensed to practice pharmacy in Massachusetts
- Name of pharmacy where respondent practiced
- Location of pharmacy (city or town)
- Brand or brands of Diethylstilbestrol (DES) ordinarily or customarily dispensed in the 5mg or 25mg size (pregnancy sizes)

For this service I will charge $800/day for four or five 5 days or $4,000 maximum. I will write a report on the findings and sign my name to the report.

Hannelore Vanderschmidt

Hannelore Vanderschmidt, PhD
Co-Director

Boston University

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Boston, Massachusetts 02215
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August 26, 2004
Mr. Harold Sparr, R.Ph., D.Ph., M.S,
P.O .Box 66
Otis, Massachusetts 01253
Dear Harold:

You have asked that I enter and analyze the responses to a questionnaire survey seeking to determine scientifically the market share in Massachusetts of the prescription drug Diethylstilbestrol (DES 5 & $25_{mg}$), in the state in the 1960's. This assignment was further detailed in a letter from Aaron M. Levine to you dated May 5, 2004 (see Attachment 4). As a practicing pharmacist of forty-five years and the former president of the Massachusetts Board of Registration in Pharmacy you have advised me that in the fifteen years between 1955 and 1970 the market for this drug remained relatively stable, although the popularity of the drug slowly decreased.

Because we are attempting to determine market shares forty years later, when so many of the pharmacists who were practicing then may have moved, retired or died, a target population of those pharmacists who were practicing in the period 1963 to 1967 was determined to the be the most reasonable population that would be both available and knowledgeable at the same time typical and timely as to this query.

I reviewed the attached questionnaire and made several suggestions, which were incorporated. (See Attachment 1). Although I was not responsible for the sample or mailing, the methods used seem scientifically valid.

I consulted and considered the following document, after approving this study design: Lilly's experts proposed testimony of market share, (Attachment 5).

I met personally with you and Peter Steere to review their familiarity and insights into the dynamics and chronology of this market and to discuss some of the challenging issues we were facing:

a. How could we insure that the memories of the target group were reliable?
b. What number of returns would constitute as sufficient sampling?
c. What were the variables in the twelve-year period under study and how did this impact on the years selected?
d. What were the prescribing habits of various physicians prescribing this drug, i.e. how was the drug prescribed?
e. What were the indications for these prescriptions?

My responsibility with respect to the survey is outlined in my letter of agreement of April 13, 2004 (Attachment 6) in broad terms, I agreed to analyze, aggregate and summarize data from the pharmacist's survey regarding dispensing of Stilbestrol/Diethylstilbestrol (DES) in the 1960's.

## Overview

A one page 11-item survey was sent to 370 currently licensed pharmacists who were originally licensed 1/1/63—6/30/67. (See Attachment 1) I received 159 responses of which 6 were duplicates. My analysis is based on the 153 unduplicated responses, a 41.4% return rate). Of these 153 responses 79 practiced in Massachusetts at some time from 1963 to 1967 (question 5) in a pharmacy which stocked DES in the pregnancy dosages (question 8). Of these 79 respondents 71 (89.9%) volunteered Lilly as the most likely brand to be dispensed (question 9), 2 (2.5%) volunteered Lilly along with other brands, 5 (6.3%) could not remember, and 1 (1.2%) volunteered a different brand (Upjohn).

Thirteen cases initially eliminated from consideration were reinstated in the follow up process.

To test statistical significance my null hypothesis is that pharmacies are as likely to dispense non Lilly DES as Lilly DES. Using the nomenclature of Ted Colton *Statistics in Medicine* (Little Brown, NY, 1974, p159) assume 0.05 is a small enough chance to reject the null hypothesis. The Lilly response p=0.899 and $\pi$=0.5. The critical ratio $z_c$=6.99. Using a two-tailed normal distribution P<0.003. The null hypothesis is rejected. In other words, the observed percentage of Lilly preference is very unlikely to come about by chance.

## Analysis Process

The survey instrument is provided as Attachment 1. The instrument contains 9 open-ended questions and 2 close-ended questions. Data from each form were transcribed to a computer file using a specially designed program. After removal of duplicates the open ended responses were reorganized on a question-by-question basis using a second specially designed program. The result is provided as Attachment 2. The close-ended questions were read into SPSS statistical software. Frequency counts and a cross tabulation are provided as Attachment 3.

## Questions 1-4

This personal address information is useful should follow up be required to clarify a response. These responses are bundled in the Section One of Attachment 2.

## Question 5

The response identifies respondents who were retail pharmacists in Massachusetts either in 1965 or in the period 1963 to 1967, depending on which questionnaire the respondent

received. Of 153 unduplicated responses, 100 answered this question "yes", 66.2% of those who answered the question. See attachment 3.

This question was originally asked "During the period 1965 ...". Later questionnaires modified the date to "1963-1967". The follow up process contacted the respondents who had received the first questionnaire and who did not answer "yes". Thirteen provided new responses that are included in the survey rather than their original responses.

## Questions 6 and 7

The response to this question identifies the name and location of the pharmacy in which the respondent practiced if the respondent answered question 5 "yes". The responses are in Section Two of Attachment 2. They represent locations widely scattered across the commonwealth.

## Question 8

The response identifies respondents whose pharmacies stocked and dispensed DES in the pregnancy dosage during the 60's. Of 153 unduplicated responses, 89 (58.2%) answered this question "yes", 78.8% of those who answered the question. See attachment 3.

## Question 9

This key question asks the respondent what brand of DES was most likely dispensed if the prescription did not name a brand. The question is open ended, providing no prompts. Only the 79 respondents who answered "yes" to both questions 5 and 8 qualified for analysis. Of the 79, 71 volunteered "Lilly" as reported above. To obtain this result Section Three of Attachment 2 containing the responses to question 9 is used. A listing of responses to questions 5 and 8 is used to identify the qualified group and the number of "Lilly" and other kinds of response are tabulated by inspection.

## Question 10

This question provides space for respondent comment. Most respondents did not comment; see Section Four of Attachment 2. A few comments relevant to the survey:

- I do remember seeing DES by Brewer & Co. and also Parke-Davis because I worked in prescription department from 1959 until became registered in 1965 but by that time I believe the DES we used was Lilly.
- I only recall the Lilly brand at that time.
- Lilly was the #1 supplier of generics then.
- Squibb was also used. I recall 5g. tabs and am pretty sure we had 25g.
- Extremely frequently prescribed by many physicians to many women or all ages.
- I believe that we only stocked Lilly's brand but I could be mistaken. That was a long time ago!

## Question 11

This question solicits the name of the wholesaler. Responses are provided in Section Five of Attachment 2. Among those frequently cited, in order of frequency of citation:

Gilman, James W. Daly, McKesson, Mass Wholesale, United Consumers, New England Wholesale.

## Conclusions

My conclusions are as follows:

1. The survey is trustworthy and based on a well-grounded sampling, considering the past time of the event we are considering.
2. Hearsay and memory risks were satisfactorily minimized.
3. The numbers of possible responders was properly surveyed to obtain a representative sample.
4. The questionnaire contained clear, precise and non-leading questions, which were answered appropriately consistent with the sources of information.
5. The responders had no knowledge of the litigation nor could they have been influenced or sympathetic to any individual or company.
6. The mailings, return receipts and collating protected the security and impartiality of the survey.
7. My statistical analysis was in accordance with accepted and standard epidemiological procedures.
8. The study and its results meet or surpass the assignment I undertook as contained in a letter to you from an attorney who I understand represents DES daughters seeking compensation from the manufacturer. (See Attachment 4). However, neither this attorney, nor anyone else engaged in such litigation nor any of the claimants have played any role in the design or conduct of this survey or my conclusions.
9. This study is adequately free from any bias that could invalidate the results.
10. The Lilly experts' opinions (Attachment 5) do not focus on the State of Massachusetts or the time period, and are therefore invalid in answering the pertinent questions.

Based on the foregoing analysis I conclude to a reasonable degree of statistical certainty and within reasonable principles of sample surveying that the Lilly brand would have been dispensed in 90 out of 100 instances in response to prescriptions for DES that did not designate a brand within the Commonwealth of Massachusetts between the years 1963 to 1967. The error in this rate is ±6. This conclusion can be extended to other years in so much as dispensing habits did not change.

Sincerely,

Hannelore Vanderschmidt

Hannelore Vanderschmidt, PhD, Ed.M
Co-Director, Center for Educational Development in Health
Adjunct Associate Professor of Public Health, Boston University

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| KIMBERLY C. CUTONE and, ANTHONY CUTONE<br><br>Plaintiffs.<br>v.<br><br>ELI LILLY AND COMPANY,<br><br>Defendant. | Civil Action No. 04-CV-12725 (JLT) |

**AFFIDAVIT OF AARON M. LEVINE, ESQ.**
**REGARDING IDENTIFICATION**

I, Aaron M. Levine, hereby declare:

1. I am the attorney for Plaintiff Kimberly Ann Wilson in this action. I am duly admitted to practice in the District of Columbia. I am fully familiar with the facts and circumstances of this case.

2. I have been engaged in DES litigation since the early 1980s.

3. I was the chairman of the DES litigation group of the Association of Trial Lawyers of America and served for most of the committee's life in that position. Affiant coordinated nationwide DES litigation and maintained contact with dozens of lawyers throughout the country who were dealing with DES litigation. I coordinated, served as clearinghouse, wrote newsletters and generally assisted in the national litigation to obtain compensation for DES daughters.

4. Affiant has published in articles on DES in legal and medical journals.

5. Affiant has personal knowledge of the legal defenses of DES manufacturers in at least 400 lawsuits. Through personal knowledge and conversations with other lawyers, Affiant has knowledge of 1,000 other DES cases.

6. The policy of my office has been to exercise transparency and provide DES manufactures, including Eli Lilly, with new developments in identification evidence during discovery.

7. In 2004, Affiant met with Mr. Harold Sparr, R. Ph. from The Massachusetts Board of Registration in Pharmacy, Mr. Peter Steere from Remedy Pharmacy Management Services, and Dr. Hannelore Vanderschmidt from Boston University, Center for Educational Development in Health to discuss the survey criteria in accordance with the Reference Guide on Survey Research", Reference Manual on Scientific Evidence, 2d ed., (Fern M. Smith ed., Federal Judicial Center 2000, pp. 229-271).

8. Dr. Vanderschmidt was able to define the survey objective, isolate and meet various challenges to the survey's validity, and determine the proper questions to be used on the questionnaire, as well as evaluate the survey sampling and administration process. She designed or approved all aspects of the questionnaire, data collection and correlation.

10. I merely memorialized the results and criteria promulgated at the meeting in the letter attached as Defendant's Exhibit 2.

11. Dr. Vanderschmidt then worked directly and exclusively with Mr. Harold Sparr and Mr. Steere, who had addresses and contacts in order to deliver and administer the survey to pharmacists. I was uninvolved in that process.

12. Dr. Vanderschmidt compiled and analyzed the survey results. I was uninvolved in that process.

13. Frequently, identification evidence points to non-Lilly defendants. In those cases, we would pursue the non-Lilly DES manufacturer of course.

14. Often, the identification evidence is so deficient that the cases are dismissed or rejected if the plaintiff cannot resort to market share liability. For example, if the mother of the plaintiff is dead or cannot remember what pill she took, and if there are no pharmacy records or live pharmacists.

15. In over 25 years of practice, we have sued a variety of DES manufacturers. Lilly, from what the numerous cases filed reflect, is in no way prejudiced or "targeted" by the Affiant.

16. However, it is also been our experience in the hundreds of DES cases in which we have been involved that the mother identifies the Lilly pills, 9 times out of 10. This ratio coincides exactly with the results of the scientific surveys we have conducted to determine the shares of the DES markets.

I declare under the penalty of perjury that the foregoing is true and correct.

/s/ Aaron M. Levine
Aaron M. Levine

Dated: July 5, 2006

# Summary ID# 2245

## Clinical Study Summary: Study H3E-MC-JMCF

## A Phase II Study of a Combination of Pemetrexed and Gemcitabine in Patients With Metastatic Breast Cancer: an NCCTG Study

Date summary approved by Lilly: 27 January 2006

**Brief Summary of Results**

- This was a single-stage Phase 2, non-randomized, open label, uncontrolled study with an interim analysis conducted to assess the efficacy and toxicity of pemetrexed (Pem) in combination with gemcitabine (Gem) in outpatient services for patients with metastatic breast cancer.
- The primary objective of this study was to assess the efficacy and toxicity of pemetrexed in combination with gemcitabine in patients with metastatic breast cancer who have received an anthracycline and a taxane.
- Of the 59 patients evaluable for primary efficacy (Tumor response population), 14 (23.7%) partial responses were reported for an objective response rate of 23.7% (95% CI: 16 to 39%). The disease was stable in 9 (15.3%) patients for greater than 6 months with a median of 11.0 months (range: 6.7 to 36.6 months).
- The median survival time was 10.3 months (95% CI: 8.3 to 18.9 months) and the 1-year survival rate was 49% (95% CI: 38 to 64%).
- The median time to progression was estimated to be 3.7 months (95% CI: 2.3 to 5.3 months).
- One death was reported during the treatment because of study disease.

- Thirty-two percent of the patients required a dose reduction after Cycle 1. and approximately 30% of patients required a dose reduction in Cycles 4 to 8.
- The most common hematological Grade 3/4 toxicity for the combination of pemetrexed and gemcitabine was neutropenia occurring in 83% of patients (17% Grade 3 and 66% Grade 4), and leukopenia occurring in 29% of patients (19% Grade 3 and 10% Grade 4).
- Thrombocytopenia was also common occurring in 27% of patients (24% Grade 3 and 3% Grade 4).
- Fatigue (17%) and dyspnea (15%) were the most common nonhematological Grade 3 or 4 toxicities, followed by rash (7%), and anorexia (5%).
- No difference in Grade 3/4 toxicities was observed among patients with different pre-therapy homocysteine levels. Eighty-nine percent (40/45) of patients had homocysteine levels of less than 10 μM at baseline.

| | |
|---|---|
| **Title of Study:** A Phase II Study of a Combination of Pemetrexed and Gemcitabine in Patients With Metastatic Breast Cancer | |
| **Investigator(s):** This multicenter study included 1 principal investigator. | |
| **Study Center(s):** This study was conducted at 12 study sites in one country. This trial was conducted through a network of cancer specialists at community clinics, hospitals and medical centers. Although there was only one PI from the research base, patients were enrolled by physicians across a number of sites. | |
| **Length of Study:** 38.6 months<br>Date of first patient visit: 20 December 2000<br>Date of last patient visit: 9 March 2004 | **Phase of Development:** II |
| **Objectives:**<br>• The primary objective of this study was to assess the efficacy and toxicity of pemetrexed (Pem) in combination with gemcitabine (Gem) in patients with metastatic breast cancer who have received an anthracycline and a taxane.<br>• The secondary objective was to describe the time to disease progression (TtPD) and the effect of treatment on overall survival (OS). | |
| **Study Design:** This was a single-stage Phase 2, non-randomized, open label, uncontrolled study with an interim analysis conducted to assess the efficacy and toxicity of Pem in combination with Gem in outpatient services for patients with metastatic breast cancer. Gemcitabine was given by intravenous (iv) infusion at a dose of 1250 mg/m$^2$ on Day 1 and Day 8 of a 21-day cycle. Pemetrexed was given by iv infusion at a dose of 500 mg/ m$^2$ after the end of gemcitabine infusion on Day 8 of a 21-day cycle. Observation for complete response (CR) patients were every 3 months for 1 year, then every 6 months until disease progression and then patients went to event monitoring phase. For patients with a partial response (PR) or had a stable disease (SD), treatment continued till progressive disease or unacceptable toxicity when patients went to the event-monitoring phase. | |
| **Number of Patients:**<br>Planned: 55 patients<br>Randomized/Enrolled: 59 Pem/Gem patients<br>Completed: 59 Pem/Gem patients | |

**Diagnosis and Main Criteria for Inclusion:** Patients were women 18 years or older with histologic or cytologic confirmed bi-dimensionally measurable breast cancer with clinical evidence of metastatic disease. Patients must have had an anthracycline and a taxane or a combination of both, in the adjuvant or metastatic setting with no more than 1 prior chemotherapy regimen for metastatic disease (unless these were a taxane and anthracycline).

**Study Drug, Dose, and Mode of Administration:**
Gemcitabine 1250 mg/m$^2$ was given intravenously (iv) over 30 minutes on Day 1 and Day 8 of a 21-day cycle.
Pemetrexed 500 mg/m$^2$/day, given iv over 10 minutes after the end of gemcitabine infusion on Day 8 of a 21-day cycle.
Folic acid 350 to 600 µg was given orally daily starting 7 days prior to the first dose of the study drugs. Folic acid was to continue daily until 3 weeks after the last dose of pemetrexed.
Vitamin $B_{12}$ was administered as a 1000 µg intramuscularly injection starting 7 days prior to the first dose of pemetrexed and repeated every 9 weeks until 3 weeks after the patient discontinued from study therapy.
Dexamethasone (4 mg twice per day) or its equivalent was taken orally on the day before, day of, and day after all doses of pemetrexed.
Anti-emetics were given before chemotherapy on Days 1 and Day 8 according to institutional guidelines.

**Duration of Treatment:** Two additional cycles of Pem/Gem would be continued if a patient had achieved a complete response. For patients with a partial response (PR) or stable disease (SD), treatment with Pem/Gem continued until the time of progressive disease or unacceptable toxicity when patients went to the event-monitoring phase. In the event of unacceptable toxicity in the absence of an objective response or patient refusal/withdrawal, the patients went to the event-monitoring phase. Follow-up continued until death or 5 years. Further follow-up was not required if a patient was still alive after 5 years after registration.

**Variables:**
Efficacy: Efficacy measures included tumor overall response rate (CR or PR rate) as defined by Response Evaluation Criteria in Solid Tumors (RECIST), and time-to-event parameters: duration of response, survival time, 1 year survival rate, SD, TtPD, and OS.
Safety: Safety measures included physical examinations, clinical laboratory tests (hematology, blood chemistries, creatinine clearance), plasma homocysteine (Hcys) level at baseline and at Cycle 2, adverse events and number of blood transfusion required. All toxicities were graded according to the National Cancer Institute Common Toxicity Criteria.

**Evaluation Methods:**
Statistical: This single stage, non-randomized Phase 2 study with an interim analysis was based on optimal two-stage designs by Simon (1989). Fifty-nine patients were enrolled in this study to evaluate tumor response rate to pemetrexed in combination with gemcitabine. Radiologic studies (roentgenograms, computed axial tomographic scans or magnetic resonance imaging) were performed at baseline and after every two cycles of therapy to assess tumor response. A treatment success was defined as either a CR or PR observed on 2 consecutive evaluations at least 4 weeks apart. This study was designed to test the null hypothesis that the true treatment success rate is at most 0.15. The smallest treatment success proportion that would imply this regimen warrants further study was 0.30. The distribution of time to progression and survival time was estimated using Kaplan-Meier analysis. Confidence intervals for the true treatment success rate were constructed according to the method of Duffy and Santer.
Homocysteine Levels: Homocysteine (Hcys) is a sensitive biomarker for folate inadequacy and a significant risk factor for treatment-related toxicities. Fifty-six patients were included in the Hcys analysis at baseline. Twenty-seven patients were included in the Hcys at Cycle 2.

**Results:**

**Patient Demographics**

A total of 59 female patients (pts) were enrolled between December 2000 and January 2003. Table 1 displays the demographics and disease characteristics of these patients. The majority of patients were white (55 pts, 93.2%). Forty-six (78.0%) patients were post-menopausal and 51 (86.4%) patients had visceral metastasis. The number of prior adjuvant chemotherapy regimens was 0 (5 pts, 8.5%) or 1 (54 pts, 91.5%). The number of prior metastatic chemotherapy regimens was 0 (23 pts, 39.0%), 1 (35 pts, 59.3%), or 2 (1 pt, 1.7%). Twenty-eight (47.5%) patients had received prior hormonal therapy.

**Table 1. Baseline Patient Demographics**

| Variable | N=59 |
|---|---|
| | n (%) |
| Median Age (range) | 51 (32-74) |
| Age Group: | |
| <40 | 10 (17.0) |
| 40-49 | 18 (30.5) |
| 50-59 | 16 (27.1) |
| 60-69 | 9 (15.3) |
| ≥70 | 6 (10.2) |
| Race: | |
| Asian | 1 (1.7) |
| Black | 3 (5.1) |
| White | 55 (93.2) |
| Performance Status: | |
| 0 | 32 (54.2) |
| 1 | 27 (45.8) |
| Dominant Disease Status: | |
| Soft tissue | 8 (13.6) |
| Visceral | 51 (86.4) |
| Bone | 0 (0.0) |
| Menopausal Status: | |
| Pre-menopausal | 13 (22.0) |
| Post-menopausal | 46 (78.0) |
| Estrogen Status: | |
| Negative | 26 (44.1) |
| Positive | 32 (54.2) |
| Unknown | 1 (1.7) |
| Progesterone Status: | |
| Negative | 25 (42.4) |
| Positive | 31 (52.5) |
| Unknown | 3 (5.1) |
| # Prior Adjuvant Regimens: | |
| 0 | 5 (8.5) |
| 1 | 54 (91.5) |
| 2 | 0 (0.0) |
| # Prior metastatic Regimens | |
| 0 | 23 (39.0) |
| 1 | 35 (59.3) |
| 2 | 1 (1.7) |
| Prior Hormomal Therapy | 28 (47.5) |

Abbreviation: n = number of patients; N = Total number of enrolled patients.

## Patient Disposition

Three hundred and sixty-two doses of treatment were administered throughout the study with a median of 5 cycles per patient (range 1 to 22). All 59 patients have discontinued study treatment. The most common reasons for discontinuing treatment include disease progression for 37 (63%) patients, adverse event for 9 (15%) patients, and patient refusal for 8 (14%) patients. One (3%) patient died during the study treatment. The indicated cause of death was due to disease progression. Figure 1 presents the disposition of all patients who enrolled into the study.

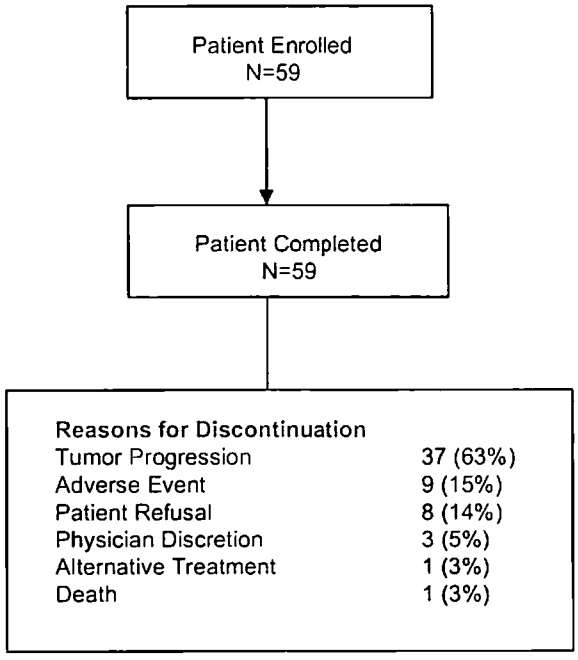


**Figure 1. Patient disposition.**

## Primary Efficacy Endpoint

Table 2 presents the objective best response data. None of the patients (0%) had a complete response (CR). Fourteen (23.7%) patients had a partial response (PR). Table 3 summarizes the overall response rate. The disease was stable in 9 (15.3%: 95% CI: 5 to 32%) patients for greater than 6 months with a median of 11 months (range: 6.7 to 36.6 months.

Table 2. Objective Best Response

| Best Confirmed Response | N=59 n (%) |
|---|---|
| CR | 0 (0.0) |
| PR | 14 (23.7) |
| SD | 9 (15.3) |

Abbreviation: CR = complete response; n = number of patients; N = total number of enrolled patients; PR = partial response; SD = stable disease.

Table 3. Summary of Overall Response Rate

| | N=59 |
|---|---|
| Overall response rate (CR + PR) (%) | 23.7 |
| 95% CI for response rate | (16 to 39%) |

Abbreviation: CI = confidence interval; CR = complete response; N = total number of enrolled patients; PR = partial response.

## Secondary Efficacy Endpoints

Table 4 summarizes the secondary efficacy endpoints of duration of response, overall survival and time to disease progression. The median duration of response was 8.3 months (range 1.6 to 16.9 months). The median survival time was 10.3 months and the 1-year survival rate was 49% (95% CI: 38 to 64%). The median time to progression was estimated to be 3.7 months (95% CI: 2.3 to 5.3 months).

Table 4. Summary of Secondary Efficacy Endpoints

| | mo | 95% CI (mo) |
|---|---|---|
| Median duration of response | 8.3 | 1.6 to 16.9 |
| Median overall survival | 10.3 | 8.3 to 18.9 |
| Median time to disease progression | 3.7 | 2.3 to 5.3 |

Abbreviations: CI = confidence interval; mo = months.

Figure 2 represents the Kaplan-Meier curves for overall survival and time to disease progression.

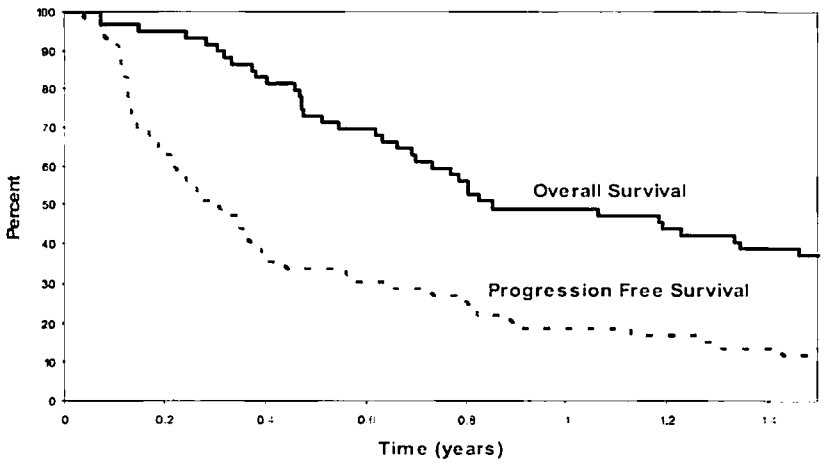


**Figure 2.** **Kaplan-Meier curves for overall survival and time to disease progression.**

## Safety

Any adverse event (AE) considered at least possibly related to treatment was defined as a toxicity. Toxicity data were available for all patients. Table 5 displays the frequency and severity of the Grade 3 and 4 toxicities occurring in at least 5% of all patients. Neutropenia was the most common and severe hematological toxicity reported with 17% of patients had Grade 3 and 66% had Grade 4. Fatigue (17%) and dyspnea (15%) were most common for non-hematological Grade 3 and 4 toxicities, followed by rash (7%) and anorexia (5%).

**Table 5.** **Common Grade 3 and 4 Toxicities Occurring in at least 5% of All Patients**

| Variables | Grade 3 (%)[a] | Grade 4 (%)[a] |
|---|---|---|
| Neutropenia | 17 | 66 |
| Leukopenia | 19 | 10 |
| Thrombocytopenia | 24 | 3 |
| Fatigue | 14 | 3 |
| Dyspnea | 12 | 3 |
| Febrile neutropenia | 12 | 2 |
| Rash | 5 | 2 |
| Anorexia | 3 | 2 |

[a] Percentage of patients with adverse events at least possibly related to study treatment.

Table 6 represents complete dose information of study drug administered during the first 8 cycles of treatment. Approximately 25% of the patients received the full dose during Cycles 5 to 8. The median dose level administered was 500 mg/m$^2$ for pemetrexed and 1250 mg/m$^2$ for gemcitabine during Cycles 1 and 2. Thirty-two percent of the patients required a dose reduction after Cycle 1, and approximately 30% of patients required a dose reduction in Cycles 4 to 8.

**Table 6. Study Drug Administered During the First Eight Cycles of Treatment**

| | Gemcitabine | | | | Pemetrexed | | |
|---|---|---|---|---|---|---|---|
| Cyc | No. of Pts on study drug | % Pts receiving full dose | % Pts receiving dose reduction during cycle | Median dose level administered (mg/m$^2$) | % Pts receiving full dose | % Pts receiving dose reduction during cycle | Median dose level administered (mg/m$^2$) |
| 1 | 59 | 91.5 | 0.0 | 1250.0 | 96.6 | 0.0 | 500.0 |
| 2 | 53 | 58.5 | 32.1 | 1250.0 | 64.2 | 32.1 | 500.0 |
| 3 | 39 | 48.7 | 17.9 | 946.4 | 51.3 | 20.5 | 473.8 |
| 4 | 37 | 40.5 | 27.0 | 938.1 | 37.8 | 27.0 | 375.2 |
| 5 | 30 | 26.7 | 30.0 | 929.0 | 26.7 | 30.0 | 370.5 |
| 6 | 27 | 22.2 | 25.9 | 904.3 | 22.2 | 25.9 | 359.1 |
| 7 | 18 | 22.2 | 27.8 | 627.2 | 22.2 | 27.8 | 246.1 |
| 8 | 16 | 25.0 | 31.3 | 706.0 | 25.0 | 31.3 | 268.5 |

Abbreviations: Cyc = cycle; No = number; Pts = patients.

Homocysteine (Hcys) levels were available for 56 patients at baseline (pre-therapy) and for 27 patients at Cycle 2. There were no significant differences observed between the median Hcys levels at baseline 8 µM (range 3 to 17) and 8 µM (range 6 to 16) at Cycle 2. Table 7 presents baseline Hcys level and toxicity distribution analysis at 10 µM Hcys level cut-off point. Eighty-nine percent (40/45) of patients with a baseline Hcys level of <10 µM and 91% (10/11) of patients with a baseline Hcys levels >10 µM experienced a Grade 3 or Grade 4 hematological toxicity (p=0.85). Similarly, 58% (26/45) of patients with a baseline Hcys levels <10 µM and 64% (7/11) of the patients with a Hcys level >10 µM had a Grade 3 or Grade 4 non-hematological toxicity (p=0.72).

Table 7. Baseline Homocysteine Level and Toxicity Distribution

| | | Toxicity | |
|---|---|---|---|
| | | Hematological Grade 3 or 4 | Non-hematological Grade 3 or 4 |
| Homocysteine level | N | n (%) | n (%) |
| ≤10 | 45 | 40 (89) | 26 (58) |
| >10 | 11 | 10 (91) | 7 (64) |
| | | (p=0.85) | (p=0.72) |

Abbreviation: N = total numbers of patient; n = number of patients; p = p-value for difference.

Volume: I
Pages: 1 to 76
Exhibits: None

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

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| | | |
|---|---|---|
| KIMBERLY C. CUTONE and ANTHONY CUTONE, Plaintiffs, | ) | CIVIL ACTION NO.: 04-CV-1365 (GK) |
| vs. | ) | |
| ELI LILLY AND COMPANY, et al., Defendants. | ) | |

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DEPOSITION OF VIRGINIA CAMPORESI
Thursday, October 27, 2005
1:12 p.m.
Held at:
Foley Hoag, LLP
Seaport World Trade Center West
155 Seaport Boulevard, 13th Floor
Boston, MA 02210-2600
Reporter: Kathryn L. Santo

A. Cramping, light spotting. I went to the doctor's.

Q. When did that start during your pregnancy?

A. Near the beginning, within the first few months.

Q. What doctor did you go see?

A. Dr. McGovern, Sr.

Q. Did you have any bleeding, apart from the light spotting, in those first --

A. No.

Q. -- few months?

A. Just spotting and the cramps.

Q. When did the spotting begin?

A. Within the second month.

Q. How long did it last?

A. Well, when I went to the doctor's -- it was a few weeks before I went to the doctor's.

Q. Did the spotting continue throughout the pregnancy?

A. No.

Q. When did it stop?

A. After I started taking the medication, the diethylstilbestrol.

there? It's halfway down the page.

MR. LEVINE: I don't see where --

MS. DWYER: It's about halfway down under "Any medications or drugs taken during pregnancy."

A. I never took aspirin. I always took Tylenol.

Q. Do you recall taking capsules for blood?

A. No. I don't even know what that is.

Q. Of the medicines that you took while you were pregnant with Kimberly, did your doctor ever give you the medicines while you were in the office, give you the actual drug?

A. No.

Q. Did you ever have any problems with these medicines while you were pregnant with Kimberly?

A. Problems? No.

Q. What were you prescribed, if anything, to help maintain your pregnancy with Kimberly?

A. Diethylstilbestrol.

Q. Who prescribed that to you?

A. Dr. Philip McGovern, Sr.

Q. How do you know he prescribed you diethylstilbestrol?

A. Because he said the word, and it was

written on the prescription.

Q. What did Dr. McGovern say to you --

A. He told --

Q. -- when he gave you the diethylstilbestrol?

A. He told me he was going to give me diethylstilbestrol to help stop my miscarriage.

Q. Had you ever had a miscarriage before?

A. No.

Q. When in your pregnancy with Kimberly did you begin taking stilbestrol?

A. It was a couple of months along.

Q. You started to tell me about what Dr. McGovern said when he first prescribed the diethylstilbestrol. Can you remember other -- what else was said during that conversation?

A. Well, I was going to have a miscarriage if I didn't take some -- you know, that medicine.

Q. Did you know what diethylstilbestrol was at the time?

A. No.

Q. What form did you take diethylstilbestrol in?

A. What do you mean?

you ever consulted with your daughter's attorney about what the pill looked like?

A. "Consulted"?

Q. Have you ever talked to your daughter's attorney about what the pill looked like?

A. When they asked me.

Q. When did they ask you?

A. When they contacted me -- when was it -- about two years ago.

Q. Who contacted you?

A. The law office, Levine.

Q. Do you remember who you spoke with?

A. Aaron Levine.

Q. What did you tell Mr. Levine when you first spoke to him about the pill?

A. I described it.

Q. How did you describe it when you first spoke to Mr. Levine about the pill?

A. It's a small, round, white pill with the cross on it.

Q. And that conversation occurred two years ago?

A. Yes, approximately.

Q. Has anyone ever showed you pictures of

A. Marcella.
Q. What was said during that conversation?
A. We discussed the medication that I took. I described the pill again.
Q. What was said about the photographs during that conversation?
A. The photographs? She asked if I recognized anything in the photographs. And I saw [redacted] it right away, the diethylstilbestrol.
Q. What did that look like in the photograph?
A. Like the pill I took.
Q. What did the photograph itself look like?
A. The photograph itself? It was a round, white pill with a crossbar on it.
Q. Were there any other pills in the picture?
A. In that picture, it was just that. There were other pictures.
Q. How many pictures did you see?
A. Oh, many. About, maybe, six pages of pictures.
Q. Was there one picture on each page, or did the pages have multiple pictures?

A. Some had multiples.

Q. Okay. Let's go through what these pictures looked like then. You said there's about six pages. So to the extent you remember, let's just start with the first page of pictures. What was on that page?

A. Many different kinds of pills.

Q. What was on the second page of pictures?

A. Same thing. Many different kinds.

Q. What was on the third page of pictures?

A. It was a picture of the -- it had pennies and a pencil, and it had the white pill with the crossbar on it. It had a couple of them.

Q. It had a couple of pills or a couple --

A. Yes.

Q. -- of other objects?

A. There were pennies, a pencil, and a bunch of the pills.

Q. What did those pills look like?

A. The round, white pill with the crossbar.

MR. LEVINE: Are you saying "bar"?

THE WITNESS: Crossbar, whatever.

MR. LEVINE: Bar?

THE WITNESS: Yes.

how you describe texture.

Q. Was the pill hard or soft?

A. Hard.

Q. Was it coated like an M&M or not coated?

A. No. No coating.

Q. Were there any markings on the pill or imprints?

A. No.

MR. LEVINE: Other than what you've previously described.

THE WITNESS: Right.

A. The cross.

Q. What did the bottle containing the diethylstilbestrol look like?

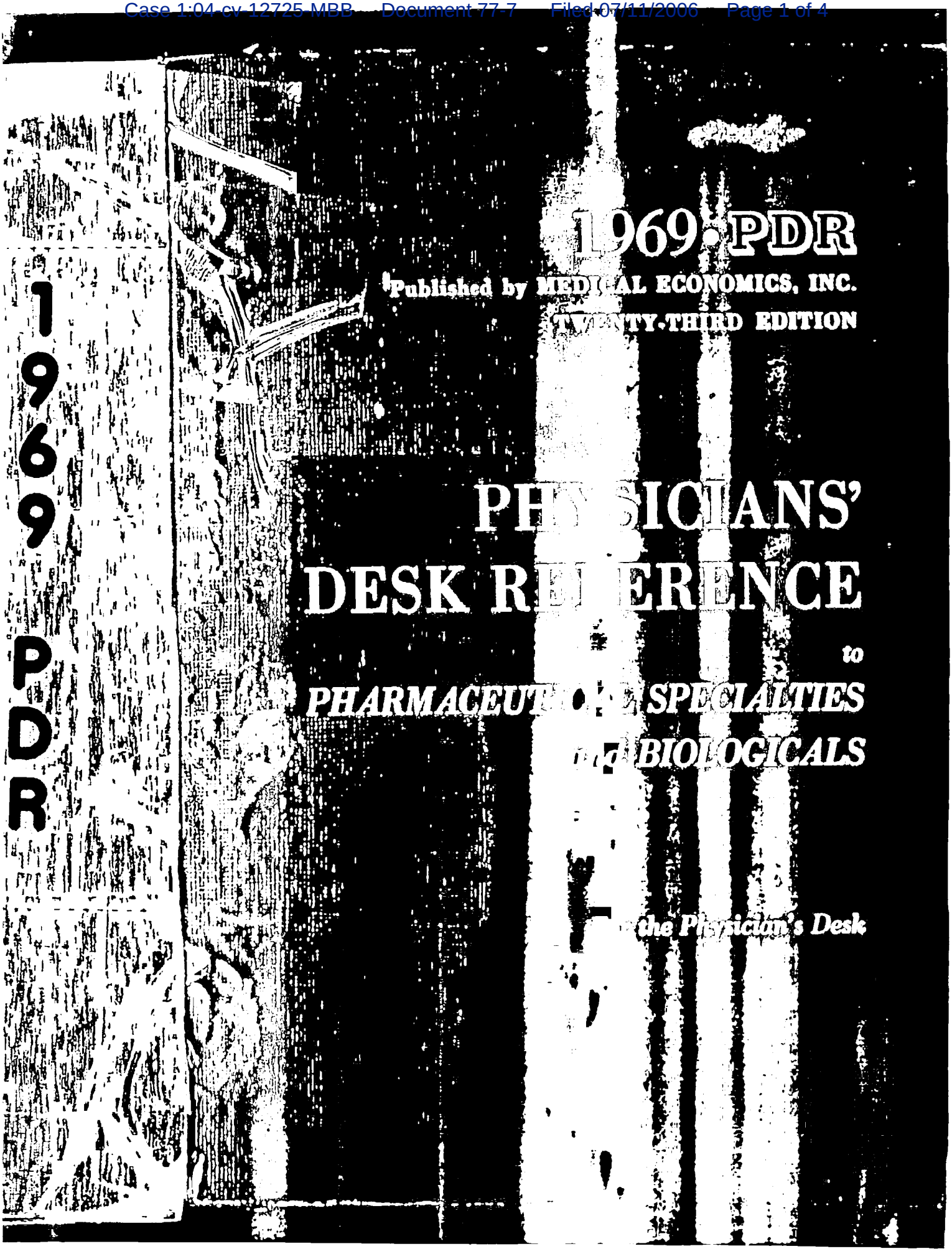
A. Just a brown bottle, brown prescription bottle.

Q. It was a brown prescription bottle from the pharmacy? Their bottle?

A. Yes.

Q. What did the label on the pharmacy bottle say?

A. It said the name of the medication, diethylstilbestrol. It had my name on it. I'm not sure of the -- the strength of the pill.


1969 PDR
Published by MEDICAL ECONOMICS, INC.
TWENTY-THIRD EDITION
PHYSICIANS'
DESK REFERENCE
to
PHARMACEUTICAL SPECIALTIES
and BIOLOGICALS
the Physician's Desk
1969
PDR

MMP Mold Allergens (Hollister-Stier)

**Glucosuria Test**

Tes-Tape (Lilly)

**Histoplasmin**

Histoplasmin (Parke, Davis)
Histoplasmin Tine Test (Lederle)

**Hypopituitarism**

Metopirone (Ciba)

**Kidney Function**

Phenolsulfonphthalein Injection (Hynson, Westcott & Dunning)

**Liver Function**

Bromsulphalein (Hynson, Westcott & Dunning)
Cardio-Green (Hynson, Westcott & Dunning)
Synkayvite Preparations (Roche)

**Myasthenia Gravis**

Mestinon Syrup (Roche)
Mestinon Tablets (Roche)
Mestinon Timespan (Roche)
Prostigmin Methylsulfate Injectable (Roche)
Tensilon (Roche)

**Pregnancy Test**

Deluteval 2X (Squibb)
Gestest Tablets (Squibb)
Pro-Duosterone (Roussel)
Prostigmin Methylsulfate Injectable (Roche)
Provera (Upjohn)

**Premature Rupture of Fetal Membranes**

Vernitest (Fuller)

**Progesterone Production**

Delalutin (Squibb)
Deluteval 2X (Squibb)
Vernitest (Fuller)

**Schick Test**

Diphtheria Toxin for Schick Test (Wyeth)
Schick Test (Wyeth)

**Stool Specimens**

Fleet Enema (Fleet)
Phospho-Soda (Fleet)

**Sugar Test Urine**

Tes-Tape (Lilly)

**Thyroid Function**

Thytropar (Armour)
Triosorb-131 (Abbott)

**Thyrotropic Hormone**

Thytropar (Armour)

**Tuberculosis**

Sterncedle (Pantay)
Tuberculin Mono-Vacc Test (Lincoln)
Tuberculin, Purified Protein Derivative (Parke, Davis)
Tuberculin Tine Test (Rosenthal) (Lederle)

**Unsaturated Iron-Binding Capacity**

Iron-Sorb-59 (Abbott)

**Vaginitis**

Nickerson's Medium (Ortho)
Vaginostic (Schmid)

---

**Diastase**

Arco-Lase (Arco)

**Diatrizoate Preparations**

Hypaque M-[illegible] (Winthrop)
Hypaque-M 90 (Winthrop)

**Diazepam**

Valium Injectable (Roche)
Valium Tablets [illegible]

**Dibucaine**

Nupercainal (Ciba)

**Dibucaine Hydrochloride**

Nupercaine Hydrochloride Ointment (Ciba)
Nupercaine hydrochloride (Ciba)
Nupercaine hydrochloride 1:3000 (Ciba)
Nuporals (Ciba)

**Dichloralphenazone**

Midrin (Carnrick)

**Dicyclomine Hydrochloride**

Bendectin (Merrell)
Bentyl Hydrochloride Filmtab Capsules, Tablets & Syrup (Merrell)
Bentyl Hydrochloride w/Phenobarbital Capsules, Tablets, Syrup (Merrell)
Kolantyl (Merrell)

**Dienestrol**

AVC Cream w/Dienestrol (National Drug)
AVC Suppositories w/Dienestrol (National Drug)
Dienestrol Cream (Ortho)
Estan (White)
Synestrol Tablets (White)

**Dietary Supplements**

*see under Amino Acid Preps., Calcium & Calcium-Phosphorus Preps., Fat Emulsions, Formula-Dietetics, Hematinics, Vegetable Oil (Preps.) & Vitamin Preps.*

**Diethylpropion**

Tenuate (Merrell)
Tenuate Dospan (Merrell)
Tepanil (National Drug)
Tepanil Ten-Tab (National Drug)

**Diethylstilbestrol**

Acnestrol Lotion (Dermik)
Dicorvin Tablets (Amide-Great)
Diethylstilbestrol (Lilly)
Furacin-E Urethral Inserts (Eaton)
Gynben Vaginal Insert & Cream (Bentex)
Quinette (Arnar-Stone)
Stilphostrol (Dome)

**Diets *(Liquid)***

LO/SO Liquid (Drug House)
Sustagen (Mead Johnson)

**Digalloyl Trioleate**

SunStick Lip Protectant (Texas Pharmacal)
SunSwept Cream (Texas Pharmacal)

**Digestants**

Arco-Lase (Arco)
Arco-Lase Plus (Arco)
Butibel-Zyme (McNeil)
Cerica-Bile Tablets (Rexall)
Cumbichole (Trout)
Convertin Tablets (Ascher)
Convertin II Tablets (Ascher)
Converzyme (Ascher)
Cotazym (Organon)
Dactilase (Lakeside)
Digestant (Cenright)
Digolase (Boyle)
Donnazyme (Robins)
Entozyme (Robins)
Enzypan (Norgine)
Festal (Hoechst)
Festalan (Hoechst)
Gastroenterase (Wampole)
Kanulyte (Dorsey)
Kanumodic (Dorsey)
Kutrase (Kremers-Urban)
Kuz-Zyme (Kremers-Urban)
Lipan (Spirt)
Mallenzyme (Mallard)
Pentazyme (Ulmer)
Phazyme (Reed & Carnrick)
Phazyme w/Phenobarbital (Reed & Carnrick)
Pro-Gestive (Nutrition Control)

**Digitalis Glycoside Preparations**

Acylanid (Sandoz)
Cedilanid (Sandoz)
Crystodigin (Lilly)
Davoxin (Davies Rose Hoyt)
Digitaline Nativelle (Fougera)
Digoxin Tablets (Rexall)
Gitaligin Tablets (Schering)
Lanoxin (B.W. & Co.)
Myodigin (Davies Rose Hoyt)
Purodigin (Wyeth)

**Digitalis Preparations**

Crystodigin (Lilly)
Davoxin (Davies Rose Hoyt)
Digitora (Upjohn)
Digoxin Tablets (Rexall)
Myodigin (Davies Rose Hoyt)
Pil-Digis (Davies Rose Hoyt)

**Digitoxin**

Crystodigin (Lilly)
Digitaline Nativelle (Fougera)
Myodigin (Davies Rose Hoyt)
Purodigin (Wyeth)

**Digoxin**

Davoxin (Davies Rose Hoyt)
Digoxin Tablets (Rexall)
Lanoxin (B.W. & Co.)
Ulti-ject Disposable Syringe (Century)

**Dihydrocodeine Bitartrate**

Drocogesic No. 3 (Century)
Synalgos Preparations (Ives)

**Dihydrocodeinone Bitartrate**

*(see under Hydrocodone Bitartrate)*

**Dihydroergotamine**

D.H.E. 45 (Sandoz)

**Dihydromorphinone Hydrochloride**

*(see also under Hydromorphone Hydrochloride)*

Dilaudid Cough Syrup (Knoll)
Dilocol (Table Rock)
Ulti-ject Disposable Syringe (Century)

**Dihydrostreptomycin Sulfate**

Kectil Suspension (Bristol)
Polymagma Suspension (Wyeth)
Polymagma Tablets (Wyeth)

**Dihydrotachysterol**

Hytakerol (Winthrop)

**Dihydroxy Aluminum Aminoacetate**

Aluscop (Westerfield)
Alzinox (Smith, Miller & Patch)
Alzinox Compound (Smith, Miller & Patch)
Donnalate (Robins)
Robalate (Robins)

**Dihydroxyanthraquinone**

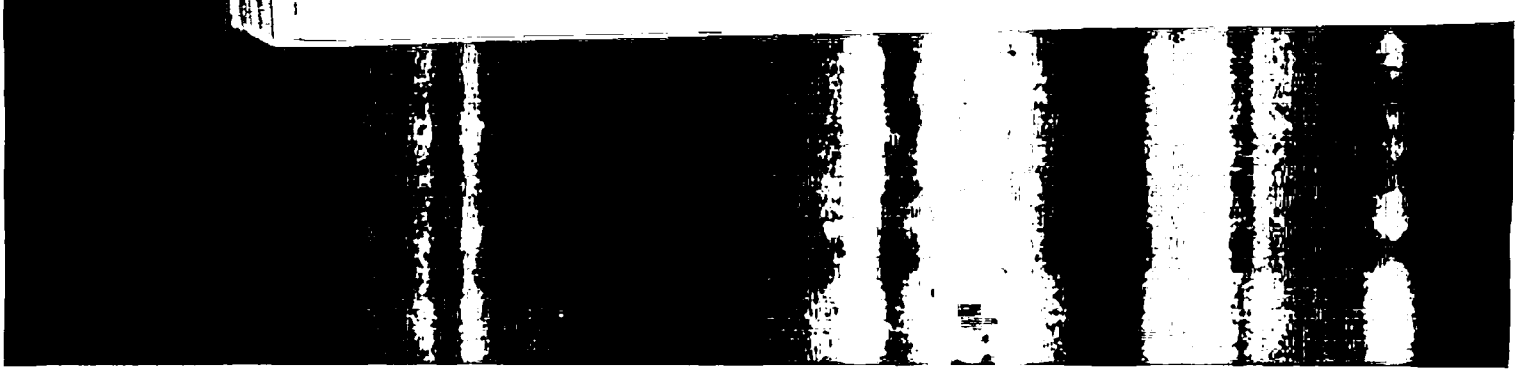
Doxan (Hoechst)
Doxidan (Hoechst)
Doxinate w/Danthron (Hoechst)

**Dihydroxyanthraquinone (1,8)**

*(See under Danthron)*

**Dihydroxypropyltheophylline**

Emfuseem Improved (Saron)



(phenaglycodol, Lilly) with the established analgesic advantages of Darvon and A.S.A. Clinical and pharmacologic studies show that Ultran enhances and prolongs the analgesic activity of Darvon when pain is accompanied by anxiety.

Each Pulvule contains—

Darvon® ..... 32 mg.
(propoxyphene hydrochloride, Lilly)
A.S.A.® ..... 325 mg.
(aspirin, Lilly)
Ultran® ..... 150 mg.
(phenaglycodol, Lilly)

Side-effects seen following administration of Darvon in adequate dosage to a large series of patients are qualitatively similar to those produced by the same or similar doses of codeine; however, from a quantitative viewpoint, the side-effects associated with Darvon are less than those of codeine.

Indications: Darvon is indicated for the reduction or amelioration of pain. It is of particular value for pain associated with recurrent or chronic disease. This is true even in such conditions as migraine, in which specific therapy sometimes fails to produce immediate or complete relief. Continued use has revealed no evidence of functional or pathological changes.

Darvon does not reduce fever or diminish inflammatory reactions.

Darvon Compound and Darvon Compound-65 provide the total analgesic effects of Darvon and A.S.A. Compound plus the anti-inflammatory and antipyretic activity of salicylates. This combination may be especially valuable in the symptomatic relief of such conditions as headache, dysmenorrhea, or various inflammatory states, e.g., arthritis and fibrositis.

Darvon with A.S.A. is made available for use by physicians who prefer an analgesic without phenacetin and caffeine.

Clinical studies indicate that the analgesic effects of Darvon are enhanced when it is given concurrently with Ultran. These studies also suggest that Darvo-Tran may provide skeletal-muscle relaxation. This presumptive evidence is based upon the fact that Darvo-Tran has been found to be more effective than Darvon per se or Darvon Compound in such diagnostic categories as arthritic conditions, tension headache, low-back syndromes, whiplash injuries, dentistry and oral surgery procedures, postpartum discomfort, and postoperative pain.

Contraindications: Although no definite contraindications to the use of Darvon have been reported, any known hypersensitivity to any of the ingredients in Darvon preparations is a contraindication. Therapeutic doses have produced no demonstrable effects on respiration, blood pressure, or reflex activity.

The presence of acute or chronic disease has not produced unusual responses during therapy with Darvon.

The concomitant administration of Darvon and orphenadrine-containing compounds is not recommended.

Caution should be exercised in the administration of Ultran to patients who are depressed.

Warnings: Salicylates should be used with caution in the presence of gastric ulcer. The prolonged and excessive use of phenacetin-containing products may aggravate or produce renal disease.

*Use in Pregnancy*—The safety of the use of Darvon during pregnancy has not been established. The potential hazards of the drug must be weighed against the possible benefits.

*Use in Children*—Darvon should not be used in children since adequate data to establish safe conditions of use are lacking.

Precautions: Patients who have received other analgesic drugs for long periods of time may have developed physical dependence on those medications. The sudden substitution of Darvon for analgesics to which patients are addicted will allow withdrawal symptoms to develop. These symptoms are not produced by Darvon and may be avoided by gradually reducing the dose of the old medication as Darvon is substituted.

Although accumulated evidence suggests that Ultran is not habit-forming or addictive, it is recommended that patients on tranquilization therapy, particularly over prolonged periods, be under periodic medical supervision. Certain patients may place inordinate dependence on any medication which alleviates discomfort, and these individuals may transgress the bounds of prescribed dosage.

Patients driving an automobile or operating hazardous machinery should be advised that mental alertness or physical co-ordination may be decreased in some persons.

The administration of Ultran with other C.N.S. depressants and/or alcohol may result in additive effects.

Adverse Reactions: Such side-effects as dizziness, headache, sedation, somnolence, paradoxical excitement and insomnia, skin rash, and gastro-intestinal disturbances (including nausea, vomiting, abdominal pain, and constipation) occur with the recommended doses of Darvon.

When recommended doses are given, euphoria and tolerance have been reported rarely. Dependence (addiction) has not been reported with therapeutic dosages.

In some instances, gastric irritation accompanying the use of Darvon Compound, Darvon with A.S.A., or Darvo-Tran may be directly attributable to the salicylate in the preparation. In such cases, it is suggested that the medication be taken with food or a small amount of milk or discontinued.

Other side-effects which have been reported with Darvo-Tran include vertigo, drowsiness, gynecomastia, headache, sedation, somnolence, insomnia, and/or excitation.

Administration and Dosage: Darvon is given orally. The usual adult dosage is 65 mg. three or four times daily; however, some physicians prefer the 32-mg. dose for certain patients. The usual dose may be given alone or with other medication, as required for the relief of pain.

The usual dosage of Darvon Compound is 1 or 2 Pulvules three or four times daily.

The usual dosage of Darvon Compound-65 or of Darvon with A.S.A. is 1 Pulvule three or four times daily.

The suggested adult dosage of Darvo-Tran is 1 Pulvule three or four times daily. When pain, with or without anxiety, is severe, 2 Pulvules three or four times daily may be indicated. It should be remembered that two Pulvules Darvo-Tran will provide a 300-mg. dose of Ultran, which may predispose to mild drowsiness in certain hypersensitive individuals. Two Pulvules also provide 64 mg. of Darvon, the amount currently recommended when moderate to severe pain exists.

Overdosage: If an overdose of Darvon is accidentally or intentionally ingested, analeptic drugs (e.g., amphetamine or caffeine with sodium benzoate) should not be used, because fatal convulsions may be produced. Animal studies and clinical experiences have demonstrated that the signs and symptoms of acute intoxication with Darvon, including muscle fasciculations, convulsions, and respiratory depression, are antagonized by nalorphine hydrochloride and levallorphan tartrate. The dosages recommended in the package literature of these antagonists should be followed and repeated as often and as long as is necessary to counteract the reappearing symptoms of overdosage.

Gastric lavage to remove unabsorbed medication is indicated. Symptomatic supportive treatment should also be given as required.

How Supplied: (R) *Pulvules Darvon® (Propoxyphene Hydrochloride Capsules, U.S.P.): No. 364 H02,** 32 mg. (No. 4, Light-Pink Opaque), in bottles of 100 and 500, in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100), and in strip packages of individually sealed Pulvules (DS1000); *No. 365, H03,** 65 mg. (No. 3, Light-Pink Opaque), in bottles of 100 and 500, in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100), and in strip packages of individually sealed Pulvules (DS1000). *Dated items.*

(R) *Pulvules No. 368, Darvon® Compound (propoxyphene hydrochloride, aspirin, phenacetin, and caffeine, Lilly), H05** (No. 0, Light-Pink Opaque Body, Light-Gray Opaque Cap), in bottles of 100 and 500, in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100), and in strip packages of individually sealed Pulvules (DS1000). *Dated item.*

(R) *Pulvules No. 369, Darvon® Compound-65 (propoxyphene hydrochloride, aspirin, phenacetin, and caffeine, Lilly), H06** (No. 0, Red Opaque Body, Light-Gray Opaque Cap), in bottles of 100 and 500, in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100), and in strip packages of individually sealed Pulvules (DS1000). *Dated item.*

(R) *Pulvules No. 366, Darvon® with A.S.A.® (propoxyphene hydrochloride with aspirin, Lilly), H04** (No. 0, Red Opaque Body, Light-Pink Opaque Cap), in bottles of 100 and 500, in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100), and in strip packages of individually sealed Pulvules (DS1000). *Dated item.*

(R) *Pulvules No. 377, Darvo-Tran® (propoxyphene hydrochloride and aspirin with phenaglycodol, Lilly), H11** (No. 0, Light-Pink Opaque Body, Maroon Opaque Cap), in bottles of 100 and 500. [030568]

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ENSEALS®, SUPPOSITORIES, AND TABLETS

Description: Diethylstilbestrol is a crystalline synthetic estrogenic substance capable of producing all the pharmacologic and therapeutic responses attributed to natural estrogens.

Indications: Tablets and Enseals Diethylstilbestrol are indicated for the relief of symptoms of the menopause; in senile vaginitis, for the relief or prevention of painful engorgement of the breasts postpartum; for control of functional uterine bleeding; in carcinoma of the prostate; and in mammary carcinoma of postmenopausal women.

Suppositories Diethylstilbestrol are indicated in postmenopausal and senile vaginitis, especially when menopausal symptoms are not present.

Contraindications: The contraindications to diethylstilbestrol administration are the same as to estrogen therapy in general. Estrogens should not be administered in the absence of a positive indication, and they should be avoided in premenopausal women with carcinoma of the breast and in all women with genital malignancy. A family history of a high incidence of breast or genital malignancy may be a contraindication.

In young patients in whom bone growth is not complete, estrogen therapy is contraindicated because of its effect on epiphyseal closure.

Suspected or known hepatic disease should be regarded as a contraindication to prolonged estrogen therapy.

Warning: Because of possible adverse reaction on the fetus, the risk of estrogen therapy should be weighed against the

*Continued on next page*

*Identi-Code® symbol—Newly manufactured capsules and tablets and the labels of powders for oral suspension and suppositories will bear Identi-Code symbols. However, a period of time will elapse before existing stocks of noncoded products are exhausted.

## Lilly—Cont.

possible benefits when diethylstilbestrol is considered for use in a known pregnancy

Precautions: Diethylstilbestrol is a potent drug, and caution must be employed in its use. Indiscriminate or injudicious administration may be dangerous. Patients receiving the drug should be under continuous medical supervision. In women, the breasts and pelvic organs should be examined before treatment is begun and at intervals during therapy.

Diethylstilbestrol should be administered with caution to a patient with bone, renal, or other disease involving calcium or phosphorus metabolism, since estrogens are known to affect metabolism of these substances. Conditions such as epilepsy, migraine, asthma, and cardiac or renal dysfunction require careful observation because the drug may produce some degree of fluid retention. Liver, thyroid, or adrenal function tests should not be performed until estrogen therapy has been discontinued for two months.

Adverse Reactions: As with natural estrogens, unpleasant side-effects have been noted following diethylstilbestrol therapy. Most common is the occurrence of nausea, which may be severe enough to lead to vomiting. The incidence of nausea appears to differ significantly among various types of patients. Pregnant and postpartum women seem the least susceptible.

Nausea and vomiting are most easily produced in the group of menopausal women. When dosage is minimal, nausea is infrequent and transient. When larger doses are given (1 mg. or more daily), and particularly when they are administered initially, nausea and vomiting are common in the menopausal group. Men and nonpregnant women form an intermediate group, nausea in them being relatively uncommon from doses of 3 to 5 mg. daily.

Continuous therapy over long periods of time, even in low dosage, may produce endometrial hypertrophy and uterine bleeding. This can be prevented in most instances by minimal dosage and by cyclic interruption of therapy when treatment must be prolonged. Porphyria cutanea tarda is also possible with prolonged use of the drug.

Other side-effects occasionally noted include abdominal distress or pain, breast tenderness and engorgement, anorexia, diarrhea, lassitude, paresthesia, vertigo, headache, anxiety, insomnia, thirst, scotomata, cutaneous rashes, purpura, and allergic reactions of various types. Side-effects may be expected to disappear on reduction of dosage or withdrawal of medication.

Administration and Dosage: *Oral*—In menopausal symptoms, 0.2 to 0.5 mg. daily, increased as needed. In senile vaginitis, 0.5 mg. daily. In painful engorgement of the breasts postpartum, 5 mg. one to three times daily for a total of 30 mg. In functional uterine bleeding, usually 5 mg. three to five times daily until bleeding ceases. In carcinoma of the prostate, 1 to 3 mg. daily, increased in advanced cases; later, the dose may be reduced to an average of 1 mg. daily. In cancer of the breast, 15 mg. daily. *Vaginal*—One 0.5-mg. suppository inserted at bedtime each night, or less frequently as needed. For maintenance, a 0.1-mg. suppository periodically may be adequate.

How Supplied: (B) *Enseals—Diethylstilbestrol Tablets, U.S.P. (Enteric): No. 46, A19,** 0.1 mg., *No. 47, A20,** 0.25 mg., *No. 48, A21,** 0.5 mg., and *No. 49, A22,** 1 mg., in bottles of 100 and 1,000; *No. 85, A33,** 5 mg., in bottles of 100, 500, and 1,000; *No. 90, A34,** 25 mg., in bottles of 100 and 500. *Dated items.*

(B) *Suppositories—Diethylstilbestrol Suppositories, U.S.P.* (Vaginal): *No. 14, S07,** 0.1 mg., and *No. 15, S09,** 0.5 mg., in packages of 6 and 50. In addition to the diethylstilbestrol, these suppositories contain glycerin, gelatin, polysorbate 20, and propylene glycol.

(B) *Tablets—Diethylstilbestrol Tablets, U.S.P.: No. 1646, J49,** 0.1 mg., in bottles of 100 and 1,000; *No. 1647, J50,** 0.25 mg., in bottles of 100; *No. 1648, J51,** 0.5 mg., and *No. 1649, J52,** 1 mg., in bottles of 100 and 1,000; *No. 1685, J54,** 5 mg., in bottles of 100 and 1,000 and in 10 strips of 10 individually labeled blisters each containing 1 tablet; *No. 1721, T70,** 25 mg. (cross-scored), in bottles of 100. *Dated items* [120467]

DIGITOXIN, *see* Crystodigin® (digitoxin, Lilly).

DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE COMBINED, *see* Tri-Solgen® (diphtheria and tetanus toxoids and pertussis vaccine combined, alum precipitated, Lilly).

• DOLOPHINE® HYDROCHLORIDE (methadone hydrochloride) Injection, U.S.P. B

AMPOULES

Description: Dolophine Hydrochloride is 4,4 - diphenyl - 6 - dimethylamino - heptanone-3 hydrochloride. It is a white, crystalline material and is water soluble. It is similar to morphine in effect, but it has a more prolonged duration of action as a result, at least partially, of greater lipid solubility.

Indications: Dolophine Hydrochloride is indicated when an analgesic effect is required, especially in the relief of postsurgical pain and pain associated with renal colic, metastatic lesions of malignant tumors, fractures, etc. When chronic administration of potent analgesics is necessary, Dolophine Hydrochloride is preferable to morphine since it induces less physical dependence. It is not recommended for the control of mild pain in place of less potent analgesic drugs, such as the salicylates or even codeine.

Contraindications and Precautions: Although Dolophine Hydrochloride has been used successfully in obstetric patients, it should be given with caution in the intrapartum period. Sedatives or other drugs which may depress fetal respiration should not be administered if delivery is anticipated before most of the drug will be eliminated from the fetal circulation. The risk is increased if the infant is premature or if general anesthesia is used for delivery.

After prolonged administration resulting in the development of considerable tolerance, withdrawal of Dolophine Hydrochloride is followed by a mild but definite abstinence syndrome.

Warning: Dolophine Hydrochloride has addictive characteristics, and a narcotic prescription is required.

Adverse Reactions: The most common side-effects produced by Dolophine Hydrochloride are nausea and vomiting. Other less bothersome symptoms include dizziness, dryness of mouth and miosis. Nausea and vomiting have appeared most often with large doses and are of the type characteristically observed following administration of morphine.

The cumulative effect of Dolophine Hydrochloride seem evident: *Although the first doses may be well tolerated, nausea may appear after several have been given. It is recommended that the drug be administered only when needed for control of pain.* Side-effects also seem to be more prominent in ambulatory patients and in those who are not suffering acute pain. In such individuals, the lower doses are advisable.

Administration and Dosage: Contents of Ampoules Dolophine Hydrochloride may be administered subcutaneously or intramuscularly.

Parenteral doses of Dolophine Hydrochloride range from 2.5 to 10 mg., according to the severity of pain, and should be repeated only when pain returns. Excessive frequency of administration and size of dose should be avoided.

Overdosage: The primary symptom of overdosage is respiratory depression. Other symptoms are drowsiness, sweating, mental depression, delirium, hallucinations, circulatory collapse, and coma. Nalorphine hydrochloride (Nallinе® HCl) provides specific therapy for overdosage. It should be repeated when necessary to counteract respiratory depression. General management should consist in symptomatic and supportive therapy, which may include administration of oxygen and intravenous fluids and maintenance of body temperature.

How Supplied: •(B) *Ampoules Dolophine® Hydrochloride (Methadone Hydrochloride Injection, U.S.P.): No. 456,* 10 mg., 1 cc., in packages of 12 and 100. Each cc. contains methadone hydrochloride, 10 mg., and sodium chloride, 0.9 percent. Sodium hydroxide and/or hydrochloric acid may have been added during manufacture to adjust the pH. *No. 435,* 10 mg. per cc., 20 cc., rubber stoppered, in single ampoules (10 per carton) and in packages of 25. Each cc. contains methadone hydrochloride, 10 mg., and sodium chloride, 0.9 percent, with chlorobutanol (chloroform derivative), 0.5 percent as a preservative. Sodium hydroxide and/or hydrochloric acid may have been added during manufacture to adjust the pH. *Dated items.*

• Narcotic order required. [021668]

• DOLOPHINE® HYDROCHLORIDE (methadone hydrochloride) B

SYRUP AND TABLETS

Description: Dolophine Hydrochloride (4,4 - diphenyl - 6 - dimethylamino - heptanone-3 hydrochloride) is an effective, stable antitussive and analgesic, 10 mg. of which are comparable in analgesic potency to morphine sulfate, 15 mg. (¼ grain).

Indications: As an antitussive, it is of benefit in the control of cough associated with the common cold, whooping cough, or chronic tuberculosis.

As an analgesic, Dolophine Hydrochloride is especially useful in relieving postsurgical pain and pain associated with renal colic, metastatic lesions of malignant tumors, fractures, etc.

Contraindications and Precautions: Although Dolophine Hydrochloride has been used successfully in obstetric patients, it should be given with caution in the intrapartum period. Sedatives or other drugs which may depress fetal respiration should not be administered if delivery is anticipated before most of the drug will be eliminated from the fetal circulation. The risk is increased if the infant is premature or if general anesthesia is used for delivery. After prolonged administration resulting in the development of considerable tolerance, withdrawal of Dolophine Hydrochloride is followed by a mild but definite abstinence syndrome.

Warning: Dolophine Hydrochloride has addictive characteristics, and a narcotic prescription is required.

Adverse Reactions: Nausea and vomiting, dizziness, dryness of mouth, and miosis may occur. Nausea and vomiting appear most often with large doses and seem to be present when the medication is given more frequently than is required to control pain (this is suggestive of cumulation). It is suggested that the drug be administered only when needed for control of pain. Side-effects seem to be more prominent in ambulatory patients and in those who are not suffering acute pain. In such individuals, the lower doses are recommended.

Administration and Dosage: *Antitussive*—Adults, 1 teaspoonful of the syrup every four to six hours (do not overdose). Children three to twelve years, ¼ to ½ teaspoonful every four to six hours (do not overdose).

*Analgesic*—Adults, moderate pain, 2.5 mg.

# ELI LILLY AND COMPANY

## Warehousing and Distribution Service Agreement

This Agreement, when executed by the Wholesaler's authorized representative and returned to, and executed by, Eli Lilly and Company (hereinafter called "Lilly") at Indianapolis, Indiana, will state the terms and conditions of the Wholesaler's agreement with Lilly for the period indicated herein.

I. **The Wholesaler Agrees:**

A. **Inventories.**

1. To purchase from Lilly and maintain at all times a complete inventory of the Lilly Products listed in the Lilly Price List (such products hereinafter called separately and collectively "Products") sufficient to supply demand, and to resort to drop-shipment orders only when necessary because of conditions beyond the Wholesaler's control.
2. To maintain the Products under proper storage conditions, including such refrigeration as may be specified by Lilly.
3. To supply only Products that are not out-of-date, damaged, or shopworn.

B. **Sales Organization.** To maintain a sales organization, including outside salesmen, adequate for personal solicitation of orders for Products in Wholesaler's trading area.

C. **Sales Effort.** To promote the Products, to give them full selling efforts and full distribution services, and not to—

1. Refuse or fail to supply promptly the Products when specified, or
2. Give preference to any other brand of products when no brand is specified.

D. **Financial Statement.** To furnish Lilly upon request a copy of its annual financial statement or other evidence of its financial condition.

E. **Automatic Shipments.** To accept automatic shipment of Products in reasonable quantities.

F. **Payment for Products.** To pay in full all invoices for Products within sixty (60) days from the date thereof.

G. **Compliance with Applicable Laws.**

1. To comply fully with all federal, state, and local laws applicable to the purchase, handling, sale, or distribution of the Products, and
2. Not to sell any narcotics, barbiturates, or other Products to any person prohibited by any federal, state, or local law from acquiring or possessing such Products.

II. **Lilly Agrees:**

A. **Shipment to Wholesaler.** To sell and ship Products (other than Products restricted to sale on a third-party basis) to the Wholesaler at the Net Wholesale prices shown in the Pricers' Edition of the Lilly Price List in effect on the date of shipment, such Net Wholesale prices being equal to the Suggested Net Trade prices specified in the Pricers' Edition of the Lilly Price List less the following discounts:

1. Group I Products—(marked "I" in the Pricers' Edition of the Lilly Price List): 16⅔%
2. Group II Products—(marked "II" in the Pricers' Edition of the Lilly Price List): 20%

B. **Special Suggested Net Trade Prices.** To adjust the net wholesale prices on Products sold and shipped from the Wholesaler's inventory on transactions for which Lilly has recommended special suggested net trade prices. The adjustments shall be made in accordance with the procedure outlined in the Lilly Chargeback Manual. Chargebacks must be properly certified and submitted to Lilly at Indianapolis, Indiana, not later than the end of the month next following the month in which the sale is made by the Wholesaler. The adjustments will result in net wholesale prices which are equal to the recommended special suggested net trade prices less the following discounts:

1. **Sales at Special Suggested Net Trade Prices (e.g., from Quotations, Quantity Price Schedule, Purchase Agreements, etc.).**

a. Total value (of each item in the case of single items or of all items in an assortment) of less than $50—

Group I Products—16⅔%

Group II Products—20%

b. Total value (of each item in the case of single items or of all items in an assortment) of $50 or more—10%

2. Sales on Special Offers (Identified as Such by Lilly).

   a. Special Offers with a total value of less than $50—
      Group I Products—16⅔%
      Group II Products—20%

   b. Special Offers with a total value of $50 or more—10%
   except that in no event shall the total annual dollar volume (at special suggested net trade prices) of sales to all Wholesalers on Special Offers providing Wholesalers a 10% discount exceed 10% of the dollar volume (at suggested net trade prices) of Lilly's total domestic sales to all Wholesalers during the previous calendar year.

   (Note: "Total value" for the purpose of subparagraphs 1. and 2. of this Paragraph B. shall be calculated on the basis of the recommended special suggested net trade prices.)

C. **Shipment to Third Parties.** To sell the Products to the Wholesaler upon third-party orders with shipment direct to the customer (i.e., drop shipments) at the applicable suggested net trade prices, regular or special, less 10%.

D. **Transportation.** To ship the Products F.O.B. Indianapolis, Indiana, transportation prepaid, subject to the following:

1. **Transportation Selected by Lilly.** Lilly will prepay that portion of the transportation charges set forth below when routing is selected by Lilly.

   a. **Shipments to the Wholesaler:**

      (1) Special Shipments. All shipments of (a) Products deferred from previous orders; (b) Products that are newly released for Wholesaler stocks (initial shipment and all reorders for first thirty [30] days after release date); and (c) allocated shipments: 100%

      (2) Regular Shipments. Shipments, other than Special Shipments, covered by the first two orders each week marked "Transportation Prepaid" by the Wholesaler: 100%

      (Note: The "first two orders each week" means the first and second orders marked "Transportation Prepaid" received by Lilly at Indianapolis, Indiana, from the Wholesaler during the period beginning at the close of business Friday and ending the following Friday at the close of business, determined on the basis of the date and time stamp placed on the order by Lilly at the time of receipt. An order for purposes of the foregoing shall include all Products in an order received by Lilly at one time and for prompt shipment, even though for the purpose of handling and shipping it is necessary for Lilly to divide it into components, e.g., biologicals, narcotics, etc.)

      (3) All other shipments to the Wholesaler: None

   b. **Shipments on Third-Party Orders:**

      (1) Products not released for Wholesaler stocks: 100%

      (2) All other Products: 50%

2. **Transportation Selected by Wholesaler.** If the Wholesaler requests special routing of a shipment which results in a higher transportation cost than would be incurred as a result of the routing of Lilly's selection, then the extra cost shall be added to the invoice.

3. **Title and Risk of Loss.** Title and risk of loss shall pass to the Wholesaler when the Products are duly delivered to the carrier.

E. **Return for Credit.** To receive from the Wholesaler for credit the Products purchased from Lilly, subject to the following:

1. All returns must be sent to Lilly at Indianapolis, Indiana, accompanied by a Merchandise Returned Form (60 DQ 9408), and must be approved by the Lilly salesman responsible for the Wholesaler, the District Manager, or other authorized representative of Lilly. Transportation for returns made upon request by Lilly shall be paid by Lilly. Transportation for all other returns shall be paid by the Wholesaler. Full credit will be allowed at the Net Wholesale prices in effect on the date of the return, except on Products damaged while in the Wholesaler's possession.

2. Undamaged Products in original containers may be returned, except biological Products prior to their date of expiration and Products marked "Nonreturnable." No credit will be allowed for parts of sales packages, in-date biological Products. or other unauthorized returns, and any that are returned will be destroyed.

3. Damaged Products for which a claim can be substantiated against a carrier may be returned when sent to Lilly at Indianapolis, Indiana, free astray via responsible carrier.

4. Products damaged in shipment, but for which claim cannot be substantiated against a carrier because the concealed damage was not discovered within the required period for inspection, may be returned, subject to inspection and approval by the Lilly salesman responsible for the Wholesaler. Return shipment is to be made apart from regular returned goods shipments.

5. Actual salvage value, if any, will be allowed on Products damaged while in the Wholesaler's possession except that no allowance will be made in case of damage by careless handling or from such perils as are normally insured under the standard fire insurance policy, including extended coverage, vandalism, and malicious mischief.

III. **General Provisions.**

A. **Orders for Products.**

1. All orders are subject to acceptance and approval by Lilly at Indianapolis, Indiana.
2. In the event of a shortage of any of the Products, Lilly shall have the right, in its sole discretion, to allocate such Products among its various wholesalers.
3. Lilly may, from time to time upon written notice to the Wholesaler, change the Group designation of any of the Products and may add or withdraw Products from any Lilly price list.
4. Lilly may, in its discretion, designate certain Products which will be supplied in shelf-carton or shipping-case quantities only.

B. **Billing and Payment.**

1. All orders for Products shall be invoiced as of the date shipped. Lilly may, at its option, grant extended dating on invoices covering initial distribution of selected new Products. Such extended dating, if granted, will be announced at the time of the initial shipment of the new Products.
2. Lilly shall render a monthly statement to the Wholesaler which will include all invoices and all credits issued by Lilly during the month. Subject to the provisions of Section III. B. 3., Lilly shall grant the Wholesaler 2 percent cash discount on the statement balance if remittances covering monthly statements in full, excluding extended dating invoices, are received by Lilly at Indianapolis, Indiana, on or before the fifteenth (15th) of the month immediately following the statement date. Otherwise, invoices shall be due net sixty (60) days from date of invoice.
3. Lilly may require that each order from the Wholesaler be accompanied by a certified check or other payment satisfactory to Lilly in an amount sufficient to cover the order less a cash discount of 2 percent in the event (a) reasonable grounds for insecurity arise with respect to the performance by the Wholesaler under this Agreement or (b) Lilly has given notice of termination of this Agreement.
4. Products shipped but not paid for at the time of the cancellation or termination of this Agreement shall be paid for in accordance with the terms of this Agreement.

C. **Inspection of Inventory.** A Lilly representative will consult with and advise the Wholesaler concerning the Wholesaler's inventory of Products and may inspect the same at all reasonable times.

D. **No Exclusive Territory.** This Agreement does not grant the Wholesaler any exclusive rights in any territory.

E. **Buyer-Seller Relationship.** The relationship created by this Agreement is a buyer-seller relationship and not an agency relationship.

F. **Change in Ownership of or Controlling Interest in Wholesaler.** The Wholesaler shall give ten (10) days' prior notice of the sale or other transfer of substantially all the assets of or a controlling interest in the Wholesaler.

G. **Direct Sales.** Lilly reserves the right to sell directly to the U. S. Government, the American Red Cross, and manufacturers.

H. **Repurchase of Stock.** Upon cancellation or termination of this Agreement, by expiration or otherwise, Lilly shall have the option to repurchase the Wholesaler's salable stock of Products at the Net Wholesale prices then in effect.

I. **Assignment.** Neither party shall assign its rights or obligations under this Agreement without first obtaining the written consent of the other party, and any attempted assignment without such written consent shall be void and of no effect.

J. **Contingencies Affecting Performance.** Neither party shall be liable for delay in performance or nonperformance caused by fire, flood, storm, earthquake, or other act of God, war, rebellion, riot, failure of carriers to furnish transportation, strikes, lockouts or other labor disturbances, act of governmental authority, inability to obtain material or equipment, or any other cause of like or different nature beyond the control of such party.

K. **Notices.** All notices under this Agreement shall be in writing and shall be considered given when delivered or mailed postage prepaid by registered or certified mail to the address of the party to whom notice is given as set forth on the next page.

L. **Termination or Cancellation.**

1. This Agreement shall terminate on June 30, 1971, unless renewed or sooner terminated as herein provided.
2. During its term this Agreement may be terminated by either party upon thirty (30) days' notice.
3. This Agreement shall terminate at the time substantially all the assets of or a controlling interest in the Wholesaler is sold or otherwise transferred to a new owner.
4. Either party may cancel this Agreement upon notice for breach by the other party of any covenant contained herein.

M. **Renewal.** At the option of Lilly and the Wholesaler, this Agreement may be renewed for successive terms of one (1) year. If the Wholesaler desires to renew, it shall send to Lilly at Indianapolis, Indiana, a written request for renewal forms before April 30. Duplicate copies of the renewal form executed by the Wholesaler shall be delivered or mailed to Lilly at Indianapolis, Indiana, not less than thirty (30) days before the expiration of any current term. If Lilly agrees to the renewal, it shall execute each renewal form and return one executed form to the Wholesaler.

N. **Entire Agreement.** This Agreement shall (1) supersede all prior contracts, agreements, and understandings between the Wholesaler and Lilly, all of which are hereby terminated, except any unexpired agency agreements between Lilly and the Wholesaler under U. S. Government contracts; (2) constitute the complete agreement of the parties; and (3) be controlling to the exclusion of all terms and conditions of the Wholesaler's purchase orders or other documents in conflict with this Agreement.

O. **Governing Law.** This Agreement shall be interpreted in accordance with, and governed by, the laws of the State of Indiana.

IN WITNESS WHEREOF, the Wholesaler has executed this Agreement and the same has become finally effective on the first day of July, 1970 upon execution at Indianapolis, Indiana, by an authorized representative of Lilly.

WHOLESALER:

.....
(NAME)

.....
(STREET)

.....
(CITY) (STATE) (ZIP CODE)

.....
(*ESTABLISHMENT REGISTRATION NUMBER)

By.....
(SIGNATURE)

.....
(TITLE)

LILLY:

ELI LILLY AND COMPANY
307 East McCarty Street
Indianapolis, Indiana 46225

By.....
(VICE-PRESIDENT)

*Number assigned by the Food and Drug Administration to the facility covered by this Agreement.